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Prognostic Value of BHCG and Local Tumor Invasion in Stage I Seminoma of the Testis

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Approximately 10–15% of patients with stage I pure seminoma of the testis have an elevated preorchiectomy serum beta human chorionic gonadotropin level [1–4]. The prognostic significance of this elevation is unknown. We performed a multi-institutional retrospective review of 332 men with stage I pure seminoma of the testis and evaluated the prognostic significance of this elevation and the prognostic value of local invasion of the primary tumor. Twenty-five of 191 evaluable patients (13%) had elevated preorchiectomy beta human chorionic gonadotropin. All normalized postoperatively and are alive without evidence of disease with a median follow-up of 50 months (range 1–124 mo). Of 191 patients, 190 (99.5%) are alive and free of disease. One patient underwent salvage chemotherapy for a chest recurrence, and he is alive and free of disease at 72 months. We conclude that elevated preorchiectomy serum beta human chorionic gonadotropin level and local invasion of the primary tumor do not portend a poor prognosis in patients with clinical stage I pure seminoma of the testis.

KEY WORDS: **beta human chorionic gonadotropin, tumor markers, radiotherapy, testicular cancer**

INTRODUCTION

Stage I pure seminoma of the testis represents one of the most successfully treated genitourinary malignancies encountered, with cure rates approaching 100%. Of these patients, 10–15% have an elevated preorchiectomy serum beta human chorionic gonadotropin (BHCG) level [1–4]. The prognostic significance of this elevation has not been clearly defined.

The extent of local microscopic invasion of the primary tumor has been associated with a more advanced initial tumor stage and poorer prognosis in nonseminomatous germ cell testicular tumors [4–6]. However, the incidence and prognostic significance of tunical, lymphatic, and vascular invasion in the primary tumor have not been defined in clinically localized, pure seminoma.

This multi-institutional retrospective review was designed primarily to assess the prognostic significance of elevated preorchiectomy serum BHCG levels in patients with clinical stage I pure seminoma. Additionally, histologic features of local invasion in the orchiectomy specimen were reviewed to evaluate the prognostic value of these findings in clinical stage I tumors.

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MATERIALS AND METHODS

A multi-institutional retrospective review of all cases of stage I seminoma of the testis diagnosed from January 1980 to December 1993 was performed. A total of 332 cases of stage I pure seminoma were found. Of these 332 cases, 191 (58%) were noted to have complete information. Inclusion criteria included pre- and postoperative serum BHCG levels and treatment by inguinal orchiectomy and infradiaphragmatic retroperitoneal radiotherapy alone. All other patients were excluded from the study. The median amount of retroperitoneal radiotherapy administered was 2,550 cGy (range 2,050–3,600).

Histologic features of local invasion were assessed in all primary tumors. The presence or absence of tunical, lymphatic, and vascular invasion had to be included to be entered into the study. Finally, the patients had to have one follow-up visit to evaluate disease status.

RESULTS

Complete clinical information was available for 191/332 (58%) patients. Twenty-five of 191 (13%) had an elevated preorchiectomy BHCG. All 25 of these patients had normalization of their serum BHCG after removal of the affected testis.

Detailed microscopic data was available for 138/191 (72%) men. Of the 138 patients with complete histologic data, 33 (24%) had local invasion. Five of these men had all three histologic findings; one patient had lymphatic and tunical invasion only and another demonstrated vascular and tunical invasion only. All seven of these men had normal preoperative BHCG. Of the remaining 26 patients, 21 had tunical invasion, 3 had lymphatic invasion, and 2 had vascular invasion.

Eighteen of 25 (72%) patients with elevated BHCG had microscopic data available. Four of 18 (22%) had tunical invasion only. One of 18 (6%) had vascular invasion only. Lymphatic invasion was not observed in this subset of patients. The remaining 13 patients had no evidence of local invasion of the tumor. Of the 120 patients with a normal preoperative BHCG, 28 (23%) had local invasion: 17 tunical, three lymphatic, and one vascular. The remaining seven were previously discussed.

Of 191 patients, 190 (99.5%) suffered no recurrences and are alive and free of disease with a median follow-up of 42 months (range 1–189 mo). One man suffered a recurrence in his chest and underwent salvage chemotherapy. He is free of disease at 72 months follow-up. His preoperative BHCG was normal, and he displayed no local invasion on microscopic examination. All 25 patients with elevated BHCG are alive without evidence of disease with a median follow-up of 50 months (range 1–124 mo).

DISCUSSION

The prognostic significance of an elevated BHCG in patients with stage I pure seminoma has been widely debated. There appears to be a small subset of these patients (10–15%) who have elevated BHCG levels at initial diagnosis prior to surgical excision. Additionally, it is known that local tumor invasion on histologic examination in nonseminomatous germ cell testicular cancers is a poor prognosticator and usually associated with a more advanced stage [4–6]. The relationship between BHCG and tumor invasion in addition to the prognostic significance of the two factors in stage I seminoma of the testis has yet to be clearly defined.

Several early studies indicated a poor prognosis with elevated pre-orchiectomy BHCG levels. Maier and Sulak [7] reported a poor prognosis in patients with seminomatous tumors with elevated urinary BHCG levels. However, detailed pathological analysis was not evident and nonseminomatous elements may have been included. Javadpour et al. [4] reported on 130 patients with testicular seminoma. They described the association of serum BHCG production and the syncytiotrophoblastic giant cell. Javadpour et al. [4] stated that there may be a worse prognosis in the patients who exhibit this histologic finding, but a larger prospective trial was necessary to evaluate the question.

Lange et al. [8] and Swartz et al. [9] observed that patients responded similarly to radiotherapy after orchiectomy regardless of the serum BHCG level. Scheiber et al. [10] reported on 51 patients with testicular seminoma and did not find a difference in outcome of those with elevated serum BHCG. In the same year, Mirimanoff et al. [11] reported 210 patients with testicular seminoma. All patients did well with primary orchiectomy and radiotherapy with 6-year follow-up. Mirimanoff et al. [11] concluded that serum BHCG elevation is not an unfavorable prognostic sign in pure seminoma of the testis.

In the largest study performed to date, Mirimanoff et al. [1] reviewed 1,169 pure seminomas and found 11% had elevated preoperative serum BHCG. Although they included all stages of pure seminoma, they found no difference in relapse-free survival between the men with normal preoperative serum BHCG and those with elevated levels.

We elected to investigate a large cohort of pure seminoma patients and included only stage I tumors. This was done to eliminate any possibility of differences in stage affecting the results of the study. Our data support the findings of Mirimanoff et al. [1] and indicate that an elevated preoperative serum BHCG is not a poor prognosticator in these patients. In addition, there does not appear

to be a positive correlation between local invasion on histologic examination and serum levels of BHCG. However, due to the excellent prognosis of all patients with stage I pure seminoma treated with orchiectomy and infradiaphragmatic radiotherapy, our findings are not surprising. Nevertheless, we report the largest series of stage I pure seminoma patients and our data corroborate the findings of Mirimanoff et al. [1], who included all stages of seminoma. Additionally, we found no positive correlation between elevated BHCG level and the risk of local tumor invasion. Finally, to assess accurately the prognostic role of increased serum BHCG and local tumor invasion, a large population of patients initially treated with surveillance for stage I seminoma would need to be studied.

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